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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
LOCKARD, JON MCCLELLAND	
ART UNIT	**PAPER NUMBER**
1647	

DATE MAILED: 05/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/509,648	CHARETTE ET AL.	
	Examiner	Art Unit	
	Jon M. Lockard	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 December 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,5-8,11,12,16-19,22,25,26 and 33-38* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,11,12,16-19,22,25,26 and 33-38* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

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DETAILED ACTION

Status of Application, Amendments and/or Claims

1. The Art Unit location of your application in the USPTO has changed. To aid in correlating any papers for this application, all further correspondence regarding this application should be directed to Art Unit 1647, Examiner Jon Lockard.

2. The amendment of 27 December 2004 has been entered in full. Claims 1-2, 7-8, 11-12, 19, 22, and 25 are amended. Claims 3-4, 9-10, 13-15, 20-21, 23-24, and 27-21 are cancelled. Claims 33-38 have been added

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

4. Claims 1-2, 5-8, 11-12, 16-19, 22, 25-26, and 33-38 are under consideration in the instant application. The claims also read upon the following species: Alzheimer's disease from the disorder group, cytokine antagonist from the agent capable of releasing morphogen activity group, 2-p-bromocinnamylaminoethyl)-isoquinolinesulfonamide from the protein kinase A inhibitor group, SEQ ID NO: 2 from the morphogen amino acid sequence group, OP-1 from the morphogen group, and retinoid receptor from the molecule that binds an endogenous ligand group.

Withdrawn Objections and/or Rejections

5. The objection to claim 9 as encompassing non-elected species as set forth at page 3 (¶3) of the previous Office Action (mailed 26 July 2004) is moot in view of Applicants cancellation of said claim (filed 27 December 2004).

6. The rejection of claims 3-4, 9-10, and 23-24 under 35 U.S.C. 112, first paragraph (Enablement), as set forth at pages 4-15 of the previous Office Action (mailed 26 July 2004) is moot in view of Applicants cancellation of said claims (filed 27 December 2004).

7. The rejection of claims 3-4, 9-10, and 23-24 under 35 U.S.C. 112, first paragraph (Written Description), as set forth at pages 15-17 of the previous Office Action (mailed 26 July 2004) is moot in view of Applicants cancellation of said claims (filed 27 December 2004).

8. The rejection of claims 3-4, 9-10, and 23-24 under 35 U.S.C. 112, second paragraph, as set forth at pages 17-19 of the previous Office Action (mailed 26 July 2004) is moot in view of Applicants cancellation of said claims (filed 27 December 2004).

9. The rejection of claims 1-2, 5-8, 11-12, 16-19, 22, and 25-26 under 35 U.S.C. 112, second paragraph, as set forth at pages 18-19 of the previous Office Action (mailed 26 July 2004) is withdrawn in part in view of the amended claims (filed 27 December 2004). Please see section on 35 U.S.C. 112, 2nd Paragraph below.

Maintained Objections and/or Rejections

Specification

10. The disclosure is objected to because of the following informalities:

11. Patent applications are referenced in the disclosure (pg 25, line 25). The status of the applications must be updated. The basis for this objection is set forth at page 3-4 of the previous Office Action (27 August 2003) and at page 3 of the Office Action of 26 July 20024. The

Examiner acknowledges that the application cited therein is still pending and notes Applicants intention to make the necessary amendments.

Claim Objections

12. The objections to claims 8, 11, 16-17, 19, and 26 (now being applied to claim 22) regarding the issue that the claims are not limited to the elected species are maintained and held in abeyance until allowable subject matter is identified.

35 USC § 112, 1st Paragraph (Enablement)

13. Claims 1-2, 5-8, 11-12, 16-19, and 22-26 remain rejected and newly added claims 33-38 are rejected under 35 U.S.C. 112, first paragraph, for reasons set forth at pages 4-15 of the previous Office Action (mailed 26 July 2004). The specification, while being enabling for a method of reducing leukemia inhibitory factor (LIF)-induced dendritic retraction comprising adding an antibody against gp130 to sympathetic neurons *in vitro* that have been treated with LIF and osteogenic protein-1 (OP-1) and wherein said antibody reduces LIF-induced dendritic retraction, *does not* reasonably provide enablement for a method for potentiating a morphogen activity, a method for potentiating dendritic growth, a method for potentiating OP-1 activity in a neuron, a method for promoting neuronal cell growth, a method for treating a disorder characterized by neuronal cell loss, or a method for treating a neurodegenerative disorder comprising administering to a mammal a composition comprising a molecule that overcomes morphogen inhibition. Additionally, the specification is enabling for a method of reducing ciliary neurotrophic factor (CNTF)-induced dendritic retraction comprising adding

phosphatidylinositol-specific phospholipase C (PI-PLC) to sympathetic neurons *in vitro* before the neurons have been treated with CNTF and osteogenic protein-1 (OP-1) and wherein said PI-PLC reduces CNTF-induced dendritic retraction. The specification is also enabling for a method of reducing the inhibitory effects of LIF on OP-1 stimulated dendritic growth comprising adding an anti-LIF antibody to sympathetic neurons *in vitro* that have been treated with LIF and OP-1 and wherein said antibody reduces the inhibition of LIF on OP-1 stimulated dendritic growth. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

14. Claims 1-2, 5-8, 11-12, 16-19, and 22-26 and newly added claims 33-38 are directed to a method for potentiating a morphogen activity in a neuron comprising contacting the neuron with a composition, the composition comprising a molecule which: (a) is a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor; and (b) overcomes inhibition of the morphogen activity *in vitro*; thereby potentiating the morphogen activity in a neuron. The claims recite a method for promoting neuronal cell growth, comprising contacting a neuron with a composition, the composition comprising a molecule which: (a) is a neuropoietic cytokine antagonist, a retinoid antagonist, or cAMP-dependent messenger pathway inhibitor, and (b) overcomes inhibition of growth-promoting effects of endogenous morphogens in vitro; thereby promoting neuronal cell growth. The claims recite that the morphogen activity is endogenous or the result of an exogenously provided morphogen. The claims also recite that the molecule that overcomes inhibition of the morphogen activity is a cytokine antagonist, more specifically a neuropoietic cytokine antagonist. The claims recite that the neuropoietic

antagonist is a LIF antagonist or a CNTF antagonist. The claims also recite that the morphogen comprises an amino acid sequence having at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, residues 330-431 of SEQ ID NO: 2. The claims recite that the molecule binds an endogenous ligand for a retinoid receptor. The claims are directed to a molecule that is a cAMP-dependent messenger pathway inhibitor, specifically a protein kinase A inhibitor ((2-p-bromocinnamylaminoethyl)-isoquinolinesulfonamide).

15. Applicant's arguments (filed 27 December 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

16. Applicants assert at page 7(¶2) of the response (filed 27 December 2004) that, while there are a number of morphogens, the known activities for these morphogens are similar enough that the assays described in the Specification of the present invention are sufficient guidance to allow practice of the claimed invention. Applicants further assert that the claims relate to potentiating morphogen activities, and do not necessitate one to determine which morphogen is being affected by the method.

17. Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner is unclear how the assays described in the Specification would provide sufficient guidance to one of skill in the art to identity target morphogens, or their associated activities, if the known activities are similar. Furthermore, while the Applicants assert that the claims relate to potentiating morphogen activities, and do not necessitate one to determine which morphogen is being affected by the method, a morphogen and any of its associated activities are inseparably linked. Furthermore, claims 6 and 7 require the determination of which morphogen is being applied and/or administered. It is noted that Applicants have amended claim 1 to recite "a

morphogen activity". However, undue experimentation would be required of the skilled artisan to determine which morphogen or its associated activity is being inhibited, and then administer a molecule selected from a genus of molecules consisting of a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor, to overcome the inhibition and potentiate the morphogens activity.

18. Applicants assert at pages 7-8 of the response that, contrary to the Examiner's observation, the Kim reference (Exhibit B) shows that activation of the ERK2/MEK1 pathway by FGF inhibits BMP-7 induced dendritic growth (Figure 8). The Applicants then assert that inhibiting ERK1/MEK1 will relieve the inhibition of effects of BMP-7. Lastly, the Applicants assert that the amended claims now recite specific molecules, therefore the experimental results of Kim (Exhibit B) are no longer applicable to the claims.

19. Applicant's arguments have been fully considered but are not found to be persuasive. The Examiner would like to point out that while Figure 9 (not Figure 8) demonstrates that FGF inhibits BMP-7-induced dendritic growth, it does not teach, nor is it found elsewhere in the reference, that inhibitors of ERK1/MEK1 overcome this inhibition. Furthermore, contrary to the Applicants assertion that the claims now recite specific molecules, namely a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor, these are not specific molecules but rather genera of molecules. In addition to being genera of molecules, they are genera that are defined not by their structure but by their activity. Therefore, a meaningful search of the scientific literature cannot be performed.

20. Applicants assert at page 8 of the response that evaluation of dosage and route of administration, in addition to the guidance given in the Specification, is considered to be standard in the art and cite Benet, Oie, and Schwartz in Goodman and Gilmans The Pharmacological Basis of Therapeutics, 9th edition, 1996, p. 1707-1711.

21. Applicant's arguments have been fully considered but are not found to be persuasive. It is noted that the claims still read on *in vivo* methods of potentiating a morphogen activity in a neuron. The limitation "overcomes inhibition of the morphogen activity *in vitro*" as recited in claims 1-2 is an inherent property of the molecule, and does not limit the "method for potentiating a morphogen activity in a neuron" to *in vitro* methods. It is further noted that Applicants have not supplied the Benet et al. reference so it has not been considered by the Examiner. Such broad brush assertions of making, screening, and administering compounds disclosed in the Specification do not constitute adequate guidance to practice the claimed method, but rather constitute an invitation to experiment to empirically determine how to practice the suggested method to obtain the therapeutic results required by the claims. The specification discloses numerous modes of administration as well as a broad range of dosage amounts (pg 22). Although Applicant submits that parameters such as dosages and timing and methods of administration of therapeutic agents may need to be optimized and that optimization is routine, there is little guidance in the specification for one skilled in the art to determine these optimal conditions. Such trial and error experimentation is considered undue. The skilled artisan must still resort to trial and error experimentation to determine the optimal dosage, duration, and mode of administration of all possible molecules that potentiate a morphogen

activity in a neuron. The claims of the instant application encompass any method of administration and any dosage for any length of time.

22. Applicants argue at pages 8-9 that the cancellation of claims 3 and 4 renders the rejection of the claims on the grounds that in vitro results are not predictive of in vivo results moot.

23. Applicant's arguments have been fully considered but are not found to be persuasive. As noted above, the claims still read on *in vivo* methods of potentiating a morphogen activity in a neuron. The limitation "overcomes inhibition of the morphogen activity *in vitro*" as recited in claims 1-2 is an inherent property of the molecule, and does not limit the "method for potentiating a morphogen activity in a neuron" to *in vitro* methods. Regarding the instant invention, one skilled in the art would not predict that the *in vitro* results with morphogens or three genera of molecules that are only described by their activity are predictive of *in vivo* results. Additionally, as was found in Ex parte Hitzeman, 9 USPQ2d 1821 (BPAI 1987), a single embodiment may provide broad enablement in cases involving predictable factors such as mechanical or electrical elements, but more will be required in cases that involve unpredictable factors such as most chemical reactions and physiological activity. See also In re Fisher, 427 F.2d 833, 839, 166 USPQ 18, 24 (CCPA 1970); Amgen Inc. v. Chugai Pharmaceutical Co. Ltd., 927 F.2d 1200, 1212, 18 USPQ2d 1016, 1026 (Fed. Cir.), cert. denied, 502 U.S. 856 (1991). The present invention is unpredictable and complex wherein one skilled in the art may not necessarily potentiate a morphogen activity in a neuron or promote neuronal cell growth *in vivo* or *in vitro* by administration and/or application of a molecule that overcomes inhibition of a morphogen activity *in vitro*.

24. Due to the large quantity of experimentation necessary to identify and screen all possible molecules (neuropoietic antagonists, retinoid antagonists, and cAMP-dependent messenger pathway inhibitors) and morphogens; to potentiate a morphogen activity in a neuron (including, for example, motor neurons, sensory neurons, glial cells, dopaminergic neurons, serotonergic neurons, oligodendrocytes, sympathetic neurons, Schwann cells, astrocytes), promote neuronal cell growth, to administer to a subject all the possible molecules; and to determine the optimal dosage, duration, and mode of administration of all possible molecules and compositions comprising a molecule-morphogen, the lack of direction/guidance presented in the specification regarding the same, the absence of working examples directed to the same, the complex nature of the invention, and the unpredictability of the effects of administering a molecule to a subject, undue experimentation would be required of the skilled artisan to make and/or use the claimed invention in its full scope.

35 USC § 112, 1st Paragraph (Written Description)

25. Claims 1-2, 5-8, 11-12, 16-19, and 22-25 remain rejected and newly added claims 33-37 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement for reasons set forth at pages 15-17 of the previous Office Action (mailed 26 July 2004). The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

26. Claims 1-2, 5-8, 11-12, 16-19, and 22-25 and newly added claims 33-37 are directed to a method for potentiating a morphogen activity in a neuron comprising contacting the neuron with a composition, the composition comprising a molecule which: (a) is a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor; and (b) overcomes inhibition of the morphogen activity *in vitro*; thereby potentiating the morphogen activity in a neuron. The claims recite a method for promoting neuronal cell growth, comprising contacting a neuron with a composition, the composition comprising a molecule which: (a) is a neuropoietic cytokine antagonist, a retinoid antagonist, or cAMP-dependent messenger pathway inhibitor, and (b) overcomes inhibition of growth-promoting effects of endogenous morphogens in vitro; thereby promoting neuronal cell growth. The claims recite that the morphogen activity is endogenous or the result of an exogenously provided morphogen. The claims also recite that the molecule that overcomes inhibition of the morphogen activity is a cytokine antagonist, more specifically a neuropoietic cytokine antagonist. The claims recite that the neuropoietic antagonist is a LIF antagonist or a CNTF antagonist. The claims also recite that the morphogen comprises an amino acid sequence having at least 70% homology with the C-terminal seven-cysteine skeleton of human OP-1, residues 330-431 of SEQ ID NO: 2. The claims recite that the neuropoietic cytokine antagonists binds an endogenous ligand for a cytokine receptor. The claims also recite the retinoid antagonist binds an endogenous ligand for a retinoid receptor. The claims are directed to a molecule that is a cAMP-dependent messenger pathway inhibitor, specifically a protein kinase A inhibitor ((2-p-bromocinnamylaminoethyl)-isoquinolinesulfonamide).

27. Applicant's arguments (filed 27 December 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

28. Applicants assert at page 10(¶2) of the response (filed 27 December 2004) that the amended claims now recite specific molecules and the specific functions that it may have.

29. Applicant's arguments have been fully considered but are not found to be persuasive. Contrary to the Applicants assertion that the claims now recite specific molecules, namely a neuropoietic cytokine antagonist, a retinoid antagonist, or a cAMP-dependent messenger pathway inhibitor, these are not specific molecules but rather genera of molecules. In addition to being genera of molecules, they are genera that are defined not by their structure but by their activity. Therefore, a meaningful search of the scientific literature cannot be performed.

30. The specification of the instant application teaches "agents that release morphogen inhibition are appreciated by persons skilled in the art to be those that interfere with or suppress known morphogen-inhibitory signaling pathways and/or morphogen-inhibitory compounds. Morphogen-inhibition releasing agents can be any of numerous compounds such as polyclonal or monoclonal antibodies, analogs, enantiomers or other inhibitors known to inhibit or interfere with the activity of morphogen-inhibitory signaling pathways and/or morphogen-inhibitory compounds" (pg 21, lines 19-24). However, the specification does not teach all possible specific molecules that overcome morphogen inhibition. The brief description in the specification of a few examples of molecules that could overcome morphogen inhibition (e.g., antibody to gp130, PI-PLC, and a LIF antibody) is not adequate written description of an entire genus of molecules.

31. *Vas-Cath Inc. v. Mahurkar*, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed"* (See page 1117). The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed" (See *Vas-Cath* at page 1116).

32. The skilled artisan cannot envision the molecules of the encompassed methods, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method. Adequate written description requires more than a mere statement that it is part of the invention. The molecule itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

33. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class.

34. Therefore, only a specific molecule (such as an anti-gp130 antibody, PI-PLC, and an anti-LIF antibody), but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

35 USC § 112, 2nd Paragraph

35. Claims 1, 5, 6, 8, 11-12, 19, 22, 25-26, 33-35, 37, and 38 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

36. The terms "morphogen activity", "a morphogen activity", and "the morphogen activity" in claims 1, 5, and 6 is a relative term which renders the claims indefinite. The terms "morphogen activity", "a morphogen activity", and "the morphogen activity" are not defined by the claims, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. It cannot be determined if "morphogen activity", "a morphogen activity", and "the morphogen activity" means for example, inducing the migration, proliferation and differentiation of progenitor cells, inducing bone morphogenesis, or repairing non-chondrogenic tissues. The basis for this rejection is set forth at pages 17-18 of the previous Office Action (mailed 26 July 2004), pages 15-16 of the Office Action of 27 August 2003, and at pages 8-9 of the Office Action of 13 November 2002.

37. Applicant's arguments (27 December 2004), as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

38. Applicants argue at page 10 of the response that claim 1 now recites "a morphogen activity", and that while a morphogen may possess many physiological activities, the known activities are well documented and defined.

39. Applicant's arguments have been fully considered but are not found to be persuasive. As indicated in the previous Office Action (27 August 2003), any and all activities may be

encompassed by the terms "morphogen activity", "a morphogen activity", or "the morphogen activity". As previously pointed out by Applicants (response filed 22 January 2004) morphogens stimulate the proliferation of progenitor cells, stimulate the differentiation of progenitor cells, stimulate the proliferation of differentiated cell, support the growth and maintenance of differentiated cells. Applicant states that morphogens can also inhibit epithelial cell proliferation. Therefore, it is not clear from the specification or the claims what activities are or are not encompassed by this term. Additionally, it is inappropriate to read limitations in the specification into the claims. The claims must independently define the invention for which patent protection is sought. Furthermore, while the known activities of specific morphogens might be well-defined, the claims encompass any activity of a morphogen which has yet to be discovered.

40. Claim 35 is rejected as being indefinite because it is unclear what is meant by the phrase "activity of OP-1". Since Osteogenic Protein 1 (OP-1) has been shown to regulate a wide array of processes, i.e., activities, it is not clear from the specification or the claims what activities are or are not encompassed by this term. Thus, the metes and bounds of the claim cannot be determined.

41. Regarding claims 35 and 38, the acronyms "OP-1" and "CNTF" renders the claims vague and indefinite. Abbreviations should be spelled out for clarity.

42. Remaining claims 8, 11-12, 19, 22, 25-26, 33-34, and 37 are rejected for depending from an indefinite claim.

Summary

43. No claim is allowed.

44. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jon M. Lockard, Ph.D.** whose telephone number is **(571) 272-2717**. The examiner can normally be reached on Monday through Friday, 8:00 AM to 6:00 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, **Brenda Brumback**, can be reached on **(571) 272-0961**.

The fax number for the organization where this application or proceeding is assigned is **571-273-8300**.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see **http://pair-direct.uspto.gov**. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at **866-217-9197** (toll-free).

JML
May 9, 2005

ROBERT S. LANDSMAN, PH.D
PRIMARY EXAMINER